REMARKS

Upon entry of the present amendment, claims 1-4, 6 and 8-12 are pending in the instant application. The specification has been amended solely to remove embedded hyperlinks and other forms of browser-executable code. Claims 1, 3, and 4 have been amended, and claim 16 has been added. Support for the claim amendments presented herein is found throughout the specification and in the claims as originally filed. For example, support for the amendments to amended claim 4 and new claim 16 is found at least at page 2, lines 18-20; page 4, lines 18-19; page 5, lines 1-2; and in claim 1 as originally filed. Support for the amendments to claims 1 and 3 is found at least at page 2, lines 15-17, and in claim 1 as originally filed. Accordingly, no new matter has been added by the amendments presented herein.

Claim Rejections Under 35 U.S.C. §§ 102(b) and 103(a)

Claims 1-4, 6, and 8-12 have been rejected under 35 U.S.C. § 102(b) as being anticipated by Bonaldo *et al.* (Genome Research (1996) 6:791-806; GenCore version search report) (referred to herein as "the Bonaldo reference" and "the Bonaldo sequence"), or alternatively, under 35 U.S.C. § 103(a) as being obvious over the Bonaldo reference and sequence. According to the Examiner, the Bonaldo reference and sequence disclose a nucleic acid comprising nucleotides 319-555 of SEQ ID NO:1 and its corresponding encoded amino acid sequence. The Examiner has also stated that, although position 251 of the Bonaldo sequence is not specified (*i.e.*, it is listed as "n"), the Bonaldo sequence "still encompasses the claimed invention 'g', or alternative[ly], it would have been obvious to one skilled in the art at the time the invention was made to select 'g' since the genus of the nucleotides are extremely small, *e.g.*, 'a, g, c, t' and exchange alternative nucleotides involves routine skill in the art." (Office Action, page 3).

The amended claims presented herein are directed to isolated nucleic acid sequences, vectors, host cells, isolated polypeptides and methods of preparing isolated polypeptides. In particular, amended claim 1 recites an isolated nucleic acid molecule that includes the nucleotide sequence of SEQ ID NO: 1, while amended claim 3 is directed to an isolated nucleic acid molecule that includes the nucleotide sequence of the complement of SEQ ID NO: 1. As amended, claim 4 is directed to an isolated nucleic acid molecule that includes an isolated coding region of the nucleotide sequence of SEQ ID NO:1, wherein the isolated coding region includes

nucleotides 319-555 of SEQ ID NO: 1, and new claim 16 recites an isolated nucleic acid molecule that includes a complementary nucleotide sequence for an isolated coding region of the nucleotide sequence of SEQ ID NO:1, wherein the isolated coding region contains the complementary sequence of nucleotides 319-555 of SEQ ID NO: 1.

As shown in Figure 1 of the as-filed specification, the nucleic acid sequences of SEQ ID NO:1 and of nucleotides 319-555 of SEQ ID NO:1 explicitly require a guanine nucleotide at position 389, while the nucleic acid sequences of the complement of SEQ ID NO:1 or the complement of nucleotides 319-555 explicitly require a cytosine nucleotide at the corresponding position.

The Bonaldo reference and sequence fail to anticipate the nucleic acid sequence of either SEQ ID NO:1 or its complement, because neither the reference nor the sequence discloses a nucleic acid sequence having a guanine nucleotide at position 251 or a cytosine nucleotide at the corresponding position in the complementary sequence. As such, the nucleic acid sequences recited by the pending claims are novel over the Bonaldo reference and sequence.

In addition, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness. A *prima facie* case of obviousness requires some suggestion or motivation, either in the reference itself or in the knowledge generally available in the art, to modify the reference to arrive at the claimed invention. The teaching or suggestion to make the claimed invention and the reasonable expectation of success must both be found in the prior art and not based on Applicants' disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See also MPEP 706.02(j). The Bonaldo reference and the Bonaldo sequence, however, do not teach or suggest the claimed invention.

First, there is no teaching or suggestion in the Bonaldo reference and/or sequence that would motivate one of ordinary skill in the art to modify the Bonaldo sequence to include a guanine nucleotide at position 251 or a cytosine nucleotide at the corresponding position in the complement of the Bonaldo sequence. The Bonaldo sequence indicates that the nucleotide at position 251 may be either a, c, t or g, which would encode an asparagine residue, a threonine residue, an isoleucine residue or a serine residue, respectively. There is no teaching in the Bonaldo sequence that one of these codons is, or would be, more preferable to produce a desired polypeptide. Thus, there is no motivation to produce a nucleic acid sequence that encodes the polypeptide shown in Figure 1, which includes a serine residue at position 24.

Second, the Bonaldo reference and/or sequence fail to describe or suggest a polypeptide comprising SEQ ID NO:1. As shown in Figure 1, the nucleic acid sequence of SEQ ID NO:1 includes 1083 nucleotides, and, therefore, a nucleic acid molecule comprising SEQ ID NO:1 may contain more than 1083 nucleotides. The Bonaldo reference, however, describes a considerably smaller nucleic acid sequence that contains only 463 nucleotides. There is no teaching or suggestion in either the Bonaldo reference or sequence that would motivate one of ordinary skill in the art to produce any nucleic acid molecule other than the disclosed sequence, let alone a significantly larger nucleic acid molecule. Thus, the Bonaldo sequence and/or reference do not render the amended claims, particularly, amended claims 1 and 3 (and their dependent claims) obvious.

Finally, neither the Bonaldo sequence nor the Bonaldo discloses or suggests an isolated coding region that corresponds to nucleotides 319-355 of SEQ ID NO:1 or the complement of nucleotides 319-355 of SEQ ID NO:1. As described in the specification, *e.g.* at page 5, lines 1-2, an "isolated" nucleic acid molecule is "separated from nucleic acids which normally flank the nucleic acid molecule in nature." Thus, the isolated coding region corresponding to nucleotides 319-355 of SEQ ID NO:1 or the complement thereof are separated from the nucleotides that normally flank these nucleotides in SEQ ID NO:1.

In contrast, the Bonaldo sequence contains a total of eight "ATG" start codons, which could encode eight different polypeptide products. (For the Examiner's convenience, a marked copy of the Bonaldo sequence (Accession No. BF550603, available from the NCBI Sequence Viewer at http://www.ncbi.nlm.nih.gov/entrez), indicating all eight start codons, is attached hereto). The Bonaldo reference and/or sequence in no way suggests an isolated nucleic acid molecule that begins at nucleotide 181 and ends at nucleotide 417 of the Bonaldo sequence (which correspond to nucleotides 319-355 of SEQ ID NO:1). Moreover, there is no teaching or suggestion in the Bonaldo sequence that one of these start codons is more preferable or that a particular polypeptide product is more desirable. Thus, there is no motivation to produce an isolated nucleic acid coding sequence that contains nucleotides 181-417 of the Bonaldo sequence. As such, the amended claims, particularly amended claim 4 and new claim 16, are not obvious over either the Bonaldo reference or the Bonaldo sequence.

Accordingly, Applicants submit that the pending claims are not obvious over the Bonaldo reference and/or sequence, and this rejection should be withdrawn.

Objection to the Specification

The Examiner has objected to the amended specification presented in Applicants' November 5, 2003 Amendment and Response. In particular, the Examiner has requested that the removal of all embedded hyperlinks and other forms of browser-executable codes from the specification in accordance with MPEP § 608.01. As Applicants have amended the specification to remove all hyperlinks and browser-executable codes, this objection should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicant respectfully submits that the pending claims are in condition for allowance. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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IDENTIFIERS

dbEST Id: **7080046**
EST name: UI-R-C1-kq-d-07-0-UI.r1
GenBank Acc: BF550603
GenBank gi: 11660333

CLONE INFO
Clone Id: UI-R-C1-kq-d-07-0-UI (5')
Source: The University of Iowa Program for Rat Gene Discovery and Mapping (Val Sheffield, Bento Soares and Tom Casavant)
Id as DNA: UI-R-C1-kq-d-07-0-UI
Id in host: UI-R-C1-kq-d-07.r1
DNA type: cDNA

PRIMERS
Sequencing: M13 Forward
PolyA Tail: Unknown

SEQUENCE

CACGAGGCACATGTGCATAGGAACATGCGGTTGTGCACACTTGTGCACAGATGCCTGGCG
TATTCATGCACCTATATAGGTGCCAACATCCCTAGCCTGCTTCCTCAGGGGGCCTTTAGG
ACCTGAGCCCTGTCATCATTTCAGACATGGGCCTTGGCCCTGAGCAGAGGCCAAGGAAGC
ATGAAGGTGCGTTCTAGGTCTTGTTTTCTCAGACCTGTTTTCCCGTTGGGGGAGGCAGGA
GGGGGCCGCANTAATACTCCATCAAGCCCATTCCAGAGAGGAGAGACACCCACCACACTC
AGAACCTCCCAAGTATGTGAGGACTTTCCTTATGGAACCCTGAGGTTCCCTCAGTTATT
TCCTGCCTGAGAAGACAAGTCAGTCTTCCATCTCTGAGCCCAGGTCTCCTAGTCTGATAG
CTGGGGCAGCCTCTCCCATTTTGCATGTCTCTTTGGTGCAGCC

Entry Created: Dec 12 2000
Last Updated: Dec 12 2000

COMMENTS

cDNA Library Preparation: M.B. Soares Lab Clone distribution: clones will be available through Research Genetics (www.resgen.com) This clone is also available through the I.M.A.G.E. Consortium at LLNL (info@image.llnl.gov). IMAGE ID= 1775573

LIBRARY
Lib Name: UI-R-C1
Organism: Rattus norvegicus
Strain: Sprague-Dawley
Develop. stage: Adult
Lab host: DH10B (Life Technologies)
Vector: pT7T3D-Pac (Pharmacia) with a modified polylinker
R. Site 1: Not I
R. Site 2: Eco RI
Description: The UI-R-C1 library is a subtracted library derived from the

UI-R-C0 library, which is a subtracted library derived from the UI-R-A1 and UI-R-E1 libraries. The UI-R-A1 library consisted of a mixture of individually tagged normalized libraries constructed from rat placenta, adult lung, brain, liver, kidney, heart, spleen, ovary, and muscle. The UI-R-E1 library consisted of a mixture of individually tagged normalized libraries constructed from 8, 12 and 18-day embryo. The tag is a string of 3-5 nucleotides present between the Not I site and the oligo-dT track which allows identification of the library of origin of a clone within the mixture. The subtracted library (UI-R-C1) was constructed as follows: PCR amplified cDNA inserts from UI-R-C0 clones from which 3' ESTs had been derived was used as a driver in a hybridization with the UI-R-C0 library in the form of single-stranded circles. The remaining single-stranded circles (subtracted library) was purified by hydroxyapatite column chromatography, converted to double-stranded circles and electroporated into DH10B bacteria (Life Technologies) to generate the UI-R-C1 library. This procedure has been previously described (Bonaldo, Lennon and Soares, Genome Research 6: 791-806, 1996)

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CITATIONS

Medline UID: 97044477
Title: Normalization and subtraction: two approaches to facilitate gene discovery
Authors: Bonaldo,M.F., Lennon,G., Soares,M.B.
Citation: Genome Res. 6 (9): 791-806 1996

MAP DATA
